DOUBLE-BLIND TRIAL OF MUCAINE IN HEARTBURN OF PREGNANCY

STUART CARNE, M.B., B.S., D.C.H.
Hammersmith, London

IT IS POSSIBLE THAT THE TERM 'heartburn' is used by patients to describe different sensations and is often accepted by their physicians without question. Heartburn should be confined to a retrosternal discomfort or pain which is usually described by the sufferer as a 'burning' sensation, or a rawness, or a tight band. It often passes in waves upwards to the throat and acid may be regurgitated. The sensation may radiate into the neck and even the jaw or to the left shoulder or arm, simulating the pain of angina.

Many patients use the term heartburn to describe regurgitation alone, without any pain; this symptom is better described as 'water-brash', although heartburn and water-brash are frequently met together in the same patients.

Aetiology

It is usually assumed that reflux oesophagitis, implying a lax cardiac sphincter or an actual hiatus hernia, or spasm of the oesophageal sphincter is the mechanism responsible for this symptom. Both elements may be present but in pregnancy the most important factor is the increase in intra-abdominal pressure and the displacement of the stomach and cardia by the growing uterus.

Diagnosis

During pregnancy the diagnosis must rest on the history. X-ray investigation of such a relatively harmless symptom as heartburn is contra-indicated. After delivery, if the symptom persists, a full examination of the upper gastro-intestinal tract should be made.

True heartburn is not likely to be confused with any other symptom during pregnancy. Angina is extremely rare at this time, and only likely to occur in patients with aortic stenosis sufficiently severe to incapacitate them generally. Peptic ulcers, if previously troublesome, are not usually active during pregnancy (Browne and Browne, 1960)

Incidence

Heartburn is a common symptom in pregnancy, but in only a small proportion of patients is it so severe that they complain of it. The great majority, perhaps more than three-quarters of expectant mothers with this symptom, obtain a degree of relief from taking domestic remedies containing antacids. In my experience, those patients who complain to their doctor of heartburn during pregnancy, have already tried simple antacids and have failed to get significant relief.

The onset of the symptom is rare before the twentieth week and usually does not appear until the third trimester. The heartburn usually persists until the baby is delivered, at which time it almost always disappears without treatment. Occasionally it is no longer felt after the thirty-seventh week when the ' baby drops '.

It appears to be a complaint found more frequently among the more anxious pregnant women, but direct questioning reveals it to be felt just as often by their more placid sisters. Possibly, as with so many ' neurotic ' diseases, the presence of anxiety or tension makes the otherwise acceptable discomfort intolerable.

Preliminary trial

However trivial the significance of the symptom, it remains important to try to alleviate as much discomfort as possible. Women have been conditioned to accept severe heartburn as one of the necessary banes of late pregnancy and doctors are too often inclined to adopt the same attitude with remarks that it will go when the baby is born. This attitude can increase the difficulties and misery of a woman, who is already extremely uncomfortable and distressed and, in my opinion, every effort should be made to relieve these painful symptoms; provided that the therapy employed is safe to both mother and child.

In view of the limited success of standard antacid therapy, a small trial was made with mucaine, an antacid gel containing 10 mg. of the topical anaesthetic oxethazaine in each 5 ml. It was claimed that this mixture was effective in heartburn of pregnancy and, although no dramatic results were expected, six pregnant women with heartburn were offered a bottle. All six obtained relief and their experience suggested that two teaspoons (8 ml.) was a satisfactory therapeutic dose. There were no apparent side-effects and the degree of symptomatic improvement produced merited a more extensive assessment.

It was appreciated that the success or otherwise of any remedy in such a self-limiting and ill-defined complaint is hard to assess and that both symptoms and effects of therapy are purely subjective. This meant that any worth-while assessment must take the form of

a double-blind trial. Such a controlled study is justified as it is the only way to show a difference compared with simple antacid therapy and it does not expose any patient to harm.

Double-blind trial

A number of bottles were prepared and numbered in pairs with one bottle of each pair containing mucaine and the other containing the identical antacid gel of aluminium and magnesium hydroxide but without any topical anaesthetic. In addition to having a number, each bottle was labelled (*a*) or (*b*) and these letters were randomly allocated to mucaine or the simple antacid. Neither I nor the patients were aware of the identity of the contents of any individual bottle.

Thirty-six consecutive pregnant women complaining of heartburn as defined in the introduction of this paper were given a pair of bottles. They were told to take the medicine from each bottle on alternate days starting with bottle (*a*) on the first day, bottle (*b*) on the second day, bottle (*a*) again on the third day and so on. In this way it was randomly determined that half of the patients started the trial with mucaine and half with the control. The dose was generally 8 ml. three times daily before meals and a further 8 ml. on retiring at night, but patients were allowed to make some adjustment themselves, where necessary. When the medication was used up the patients returned and were asked for their preference, bearing in mind relief of symptoms and any disturbing side-effects produced. The degree of symptomatic relief and any mention of side-effects was also noted.

One small refinement was added to the trial as outlined above. It occurred to me that the mere fact of asking for a preference might create an artificial difference between the two treatments and, as an experiment, four patients were given a pair of bottles with the anaesthetic containing mucaine in both bottles. None of the patients knew that they might be getting the same medication in both containers and I did not know which patients had been given identical therapy throughout the trial. I did, however, know that these four identical pairs had been included in the trial and, to this limited extent, I was not completely ' blind '. This knowledge, nevertheless, made me more willing to accept a ' no preference ' assessment and it was explained to patients, who were reluctant to express a preference, that bottles (*a*) and (*b*) might possibly have contained the same mixture.

Results

There were really three groups of patients; those who took mucaine first, those who took simple antacids first and those who took mucaine all the time. The preference given by these groups

is given in the table.

	Total Nos.	*Prefers antacids with oxethazaine*	*Prefers antacids alone*	*No Preference*	*Preferred one of the identical bottles*	*Failed to return*
Mucaine taken first	16	14	0	2	—	0
Antacids alone taken first ..	16	14	1	0	—	1
Mucaine taken both times ..	4	—	—	3	1	0

One of the patients preferring mucaine and the patient preferring simple antacids stated that neither bottle had been fully successful in relieving their symptoms of heartburn. The remainder said that they had obtained complete relief of heartburn when taking the medication for which they had declared a preference and only partial or no relief from the other bottle.

Side-effects

Several mothers mentioned a slight discomfort in the throat after taking the more effective mixture and this was presumably due to the local anaesthetic effect. Apart from this, there were no side-effects reported by the 41 patients who took the active medication and reported their results. The patient who did not return to say which bottle was better left the district and had her baby elsewhere.

The risks of any drug administered during pregnancy causing malformations in the young have always to be considered, especially in the case of newly-introduced therapeutic substances. However, all the evidence indicates that the only danger period to the foetus is during the first trimester of pregnancy (*Lancet*, 1962); a drug will only act as a teratogenic agent when given during the period of differentiation (Woollam, 1962). Heartburn usually only occurs after the twentieth week, when these hazards are over. It would be unwise to use anything but a plain antacid before the thirteenth week. To be safe (as in cases where a period of amenorrhoea is followed by a conception, so that the duration of pregnancy is shorter than that calculated) no untried drug should be administered before the fundus is easily palpable above the symphysis pubis.

Comment

This double-blind trial demonstrates very clearly the effectiveness of oxethazaine in antacid gel in relieving the symptoms of heartburn

of pregnancy. Complete relief was obtained in 27 out of 31 cases and the improvement was so much better than that obtained with simple antacids that 28 out of 31 were able to give a preference for mucaine as opposed to an apparently identical mixture of simple antacids. The validity of the preference was further demonstrated by the fact that three out of four patients who took identical mixtures were unable to distinguish between them. Admittedly, the discomfort in the throat caused by the topical anaesthetic allowed the active material to be recognized in some cases, but this is inherent in this type of medication and cannot be overcome.

One patient, who is herself a general practitioner, remarked that the bottle she preferred not only gave more relief than the other bottle but that the improvement lasted much longer. Three expectant mothers, who had not been asked to take part in the trial, spontaneously asked for some of the medicine which they had heard about from their friends as being so effective in heartburn.

Summary

A combination of the topical anaesthetic oxethazaine in aluminium and magnesium hydroxide gel (mucaine) has been recommended for the treatment of heartburn in pregnancy.

After a preliminary trial in six patients with encouraging results a double-blind study was conducted on 32 patients with this symptom. One patient failed to return. Of the remaining 31 patients, 28 preferred mucaine and 27 declared that it produced complete relief of symptoms.

As a separate experiment, four patients were given two bottles containing mucaine and three of the four declared no preference for either medication.

Mucaine appears to be a significant improvement over simple antacid therapy for the treatment of heartburn in pregnancy.

Acknowledgements

I would like to thank John Wyeth & Brother Ltd., for supplying materials for this trial and for labelling and coding which enabled it to be double-blind.

I would like to thank Professor J. C. McClure Browne and Mr T. L. T. Lewis for their help in the preparation of this paper.

REFERENCES

Browne, F. J. and Browne, J. C. McClure (1960). *Antenatal and Postnata Care.* 9th Ed. London.

Lancet (1962). **2**, 337.

Woollam, D. H. M. (1962). *Brit. med. J.* **2**, 236.